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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/863,849	05/23/2001	Jerome O. Cantor	C35795/125237	1932

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EXAMINER	
HENRY, MICHAEL C	
ART UNIT	PAPER NUMBER
1623	

MAIL DATE	DELIVERY MODE
12/10/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/863,849	CANTOR ET AL.	
	Examiner	Art Unit	
	MICHAEL C. HENRY	1623	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *25 August 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *31-33 and 37-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *31-33, 37-47* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The following office action is a responsive to the Amendment filed, 08/25/08.

The amendment filed 08/25/08 affects the application, 09/863,849 as follows: The rejections made under 35 U.S.C. 103(a) in the prior office action mailed 02/25/08 are maintained.

1. The responsive to applicants' arguments is contained herein below.

Claims 31-33, 37-47 are pending in application

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 31-33, 37-47 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cantor (US 5,633,003) in combination with Green (WO 96/19968).

In claim 31, applicant claims "A system comprising: a mixture comprising a polysaccharide having a molecular weight of between about 50,000 and 1.5 x 10^6 Daltons at a concentration of less than about 5.0 mg/ml (w/v) of polysaccharide, and a breathable fluorocarbon propellant; a canister adapted to contain said mixture under pressure; a valve connected to said canister for regulating delivery of said mixture; and a nozzle interconnected with said valve for transforming said mixture under pressure into an inhalable aerosol mist when said valve is actuated." Dependent claim 32 is drawn to said composition or system comprising the polysaccharide in the aerosol mist is of specific median mass distribution sizes. Claim 33

and 37 are drawn to said system or composition wherein the said mixture further comprises a drug and specific drugs. Claims 34, 37-40, 42, 43, 45-47 are drawn to said system or composition wherein the polysaccharide is chemically modified, wherein the said solution further comprises a drug and specific drugs, wherein the polysaccharides are specific polysaccharides and are of specific molecular weights. Claim 41 is drawn to said system wherein a drug is conjugated to the polysaccharide.

Cantor discloses a system for delivering a polysaccharide formulation to a respiratory tract of a mammal, comprising: a mixture comprising a polysaccharide (hyaluronic acid), that can be delivered via a route aerosol inhalation by a nebulizer (see col. 3, METHODS, lines 46 to col. 4, line 45; also, see abstract). In addition, Cantor uses the same method of delivery (aerosol inhalation) for the same purpose (i.e., treating respiratory disorders) comprising a polysaccharide. Furthermore, it should be noted that the nebulizer contains the said canister, valve and nozzle, claimed by applicant. Also, Cantor discloses that the hyaluronic acid used may be derived from bovine sources, rooster comb, human umbilical cord, or streptoccus zoepidicus (see col. 3, lines 13-18). This implies that hyaluronic acid of different molecular weights can be used since the said sources of hyaluronic acid produces hyaluronic acid of different molecular weight. In fact, the hyaluronic acid suggested by Cantor are naturally occurring hyaluronic acid (i.e., hyaluronic acid from bovine sources, rooster comb, human umbilical cord, or streptoccus zoepidicus (see col. 3, lines 13-18) which are known to have molecular weight of 50,000-13,000,000 daltons (for example, see US 4,746,504: col. 4, lines 44-49). It should be noted that this molecular weight range of hyaluronic acid encompasses the molecular weight range of the hyaluronic acid claimed by applicant.

Green discloses an aerosol formulation for administration by inhalation containing a medicament, a sugar (a carbohydrate) and a fluorocarbon propellant for treating respiratory disorders (see abstract). Green discloses that the medicament can include drugs such as terbutaline, penicillins, ephedrine (see page 2, line 22-page 3, line 9). It should be noted that Green, like Cantor, also uses the same method of delivery (aerosol inhalation) for the same purpose (i.e., treating respiratory disorders). Furthermore, Green discloses that fluorocarbons can be used and are commonly used as propellants for medicinal aerosol formulations (see page 1, lines 6-21, especially lines 16-21).

The difference between applicants' claimed composition and the composition of Cantor is that Cantor does not disclose the concentration, molecular weight or particle size of the polysaccharide and cantor does not use a drug or propellant. However, Cantor suggests that hyaluronic acid from different sources (i.e., hyaluronic acid from bovine sources, rooster comb, human umbilical cord, or streptoccus zoepidicus (see col. 3, lines 13-18)) which are known to have different molecular weights can be used and Green discloses that drugs such as terbutaline, penicillins, ephedrine and a propellant such as a fluorocarbon can be used as an inhalant in the inhalant aerosol formulation (see page 2, line 22-page 3, line 9; see abstract) and that said fluorocarbon propellants are commonly used as propellants for medicinal aerosol formulations (see page 1, lines 6-21, especially lines 16-21).

It would have been obvious to one having ordinary skill in the art, at the time the claimed invention was made to have prepared the composition (an inhalant aerosol formulation) of Cantor comprising different concentrations, molecular weights or particle size of the polysaccharide in combination with a drug disclosed by Green such as terbutaline, penicillins,

ephedrine and a fluorocarbon propellant to be used as an inhalant aerosol formulation for treating respiratory conditions or disorders, depending on factors such as the severity of the respiratory disorder or the type, age and weight of subject treated, since Cantor suggests that different molecular weights of hyaluronic acid (polysaccharide) can be used and Green disclose that drugs such as terbutaline, penicillins, ephedrine and a fluorocarbon propellant can be used as an inhalant aerosol formulation and that said fluorocarbon propellants are commonly used as propellants for medicinal aerosol formulations.

One having ordinary skill in the art would have been motivated, to prepare the composition (an inhalant aerosol formulation) of Cantor comprising different concentrations, molecular weights or particle size of the polysaccharide in combination with a drug disclosed by Green such as terbutaline, penicillins, ephedrine and a fluorocarbon propellant to be used as an inhalant aerosol formulation for treating respiratory conditions or disorders, depending on factors such as the severity of the respiratory disorder or the type, age and weight of subject treated, since Cantor suggests that different molecular weights of hyaluronic acid (polysaccharide) can be used and Green disclose that drugs such as terbutaline, penicillins, ephedrine and a fluorocarbon propellant can be used as an inhalant aerosol formulation and that said fluorocarbon propellants are commonly used as propellants for medicinal aerosol formulations. More specifically, it is obvious to combine individual compositions taught to have the same utility to form a new composition for the very same purpose. In re Kerkhoven, 626 F.2d 846, 205 U.S.P.Q. 1069 (C.C.P.A. 1980). It should be noted that it is obvious to use other polysaccharides such including polysaccharides that are conjugated to a drug since both Cantor disclose the use of polysaccharides in general.

Response to Arguments

Applicant's arguments with respect to claim 31-33, 37-47 have been considered but are not found convincing.

The applicant argues that art subsequent to Cantor (the patent cited in the present rejection) reports that low molecular weight hyaluronic acid *(e.g.,* less than 250 kDa) may be pro-inflammatory. Cantor was filed in 1994 and issued in 1997. Horton and McKee published in 1999 and 1996, respectively. Following the publication of Horton in 1999, one skilled in the art would recognize at least these two reports evidencing a pro-inflammatory response associated with low molecular weight hyaluronic acid. However, the rejection set forth above was not made by applying Horton and McKee references. Moreover, Cantor does not report or disclose that low molecular weight hyaluronic acid *(e.g.,* less than 250 kDa) may be pro-inflammatory. In addition, it should be noted that applicant's claimed composition does not exclude polysaccharide with molecular weight greater than 250 kDa (e.g., see claim 31). Also, Cantor suggests that hyaluronic acid from different sources (i.e., hyaluronic acid from bovine sources, rooster comb, human umbilical cord, or streptoccus zoepidicus (see col. 3, lines 13-18) which are known to have different molecular weights can be used. Furthermore, one of ordinary skill in the art would be motivated to determine the most effect aerosol form of the hyaluronic acid composition that is administered to a patient. Again, it must be re-emphasized that the rejection set forth above was not made by applying Horton and McKee references and that any teaching of Horton and McKee references which relates to a pro-inflammatory response that may be associated with low molecular weight hyaluronic acid is irrelevant. It should also be noted that the reference of Horton and McKee references which were presented on the IDS dated 11/23/07

were previously considered by the examiner as indicated on the signed 1449 form mailed 02/25/08.

The applicant argues that in view of Horton and McKee, one skilled in the art would be led away from the presently claimed invention. However, the rejection set forth above was not made by applying Horton and McKee references. Moreover, Cantor does not report or disclose that low molecular weight hyaluronic acid *(e.g.,* less than 250 kDa) may be pro-inflammatory. In addition, it should be noted that applicant's claimed composition does not exclude polysaccharide with molecular weight greater than 250 kDa (e.g., see claim 31). Also, Cantor suggests that hyaluronic acid from different sources (i.e., hyaluronic acid from bovine sources, rooster comb, human umbilical cord, or streptoccus zoepidicus (see col. 3, lines 13-18) which are known to have different molecular weights can be used. Furthermore, one of ordinary skill in the art would be motivated to determine the most effect aerosol form of the hyaluronic acid composition that is administered to a patient. Again, it must be re-emphasized that the rejection set forth above was not made by applying Horton and McKee references and that any teachings of Horton and McKee references which relates to a pro-inflammatory response that may be associated with low molecular weight hyaluronic acid is irrelevant.

The applicant argues that with respect to Horton and McKee, a *pro-inflammatory response in the airways* in connection with a system *for inhalable delivery* of the recited polysaccharide, the utility of which is *for treating or ameliorating the symptoms of a respiratory disorder,* is not fairly characterized as a "side effect," but rather, is in contradiction with the very purpose of the claimed system. However, the rejection set forth above was not made by applying Horton and McKee references. Moreover, Cantor does not report or disclose that low molecular

weight hyaluronic acid *(e.g.,* less than 250 kDa) may be pro-inflammatory. In addition, it should be noted that applicant's claimed composition does not exclude polysaccharide with molecular weight greater than 250 kDa (e.g., see claim 31). Also, Cantor suggests that hyaluronic acid from different sources (i.e., hyaluronic acid from bovine sources, rooster comb, human umbilical cord, or streptoccus zoepidicus (see col. 3, lines 13-18) which are known to have different molecular weights can be used. Furthermore, one of ordinary skill in the art would be motivated to determine the most effect aerosol form of the hyaluronic acid composition that is administered to a patient. Again, it must be re-emphasized that the rejection set forth above was not made by applying Horton and McKee references and that any teachings of Horton and McKee references which relates to a pro-inflammatory response that may be associated with low molecular weight hyaluronic acid or whether or not the said pro-inflammatory response is a side effect, is irrelevant.

The applicant argues that motivation to attain the claimed invention based on Cantor is lacking as Horton and McKee indicate that the claimed system for inhalable delivery of the recited polysaccharide for treating or ameliorating the symptoms of respiratory disease would become inoperable or have its intended function obliterated in view of a pro-inflammatory response as disclosed by Horton and McKee. However, the rejection set forth above was not made by applying Horton and McKee references. Moreover, Cantor does not report or disclose that low molecular weight hyaluronic acid *(e.g.,* less than 250 kDa) may be pro-inflammatory. In addition, it should be noted that applicant's claimed composition does not exclude polysaccharide with molecular weight greater than 250 kDa (e.g., see applicant's claim 31) and Cantor's disclose that that their composition comprising said polysaccharide treats respiratory

disorders (i.e., it is operable). Also, Cantor suggests that hyaluronic acid from different sources (i.e., hyaluronic acid from bovine sources, rooster comb, human umbilical cord, or streptoccus zoepidicus (see col. 3, lines 13-18) which are known to have different molecular weights can be used. Furthermore, one of ordinary skill in the art would be motivated to determine the most effect aerosol form of the hyaluronic acid composition that is administered to a patient. Again, it must be re-emphasized that the rejection set forth above was not made by applying Horton and McKee references and that any teachings of Horton and McKee references which relates to a pro-inflammatory response that may be associated with low molecular weight hyaluronic acid or whether or not the said pro-inflammatory response is a side effect, is irrelevant.

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael C. Henry whose telephone number is 571-272-0652.

The examiner can normally be reached on 8.30am-5pm; Mon-Fri. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia A. Jiang can be reached on 571-272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael C. Henry
December 1, 2008.

/Shaojia Anna Jiang/
Supervisory Patent Examiner
Art Unit 1623